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EOX for Noninvasive Physiologic Monitoring

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13. ABSTRACT *(Maximum 200 words)*

An EOX is an instrument that scans low-powered lasers into a subject's eye and spectroscopically determines oxygen saturation of blood within the retinal veins and arteries. Pilot animal studies performed by our group with an EOX indicate that retinal venous oxygen saturation is a sensitive indicator of blood loss. We have developed a 2-D scanning EOX which is readily reconfigured to operate at various wavelengths, and to use confocal techniques and polarization to constrain the potential sources of collected light. Thus, the instrument is being used to fully explore the physics of retinal oximetry, with the goal of a calibrated instrument. The parallel development of a model eye allows for rapid verification of EOX modifications on a test object with far fewer unknowns. Data collection across varying oxygen saturation, hemoglobin concentration, vessel diameter, fundus reflectivity, and filtering configurations permits analysis of the contributions of each of these components to the actual complex measurement . This data has been critical to improving our understanding of the algorithms necessary for calibrating the EOX. Finally, a human pilot study performed on subjects in a Lower Body Negative Pressure experiment was also accomplished, successfully acquiring data on 15/15 subjects.

14. SUBJECT TERMS **retinal oximetry, non-invasive monitoring, calibration, hemorrhage, resuscitation**

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Final Report

GRANT TITLE: EOX for Noninvasive Physiologic Monitoring

PRINCIPAL INVESTIGATOR: Dr. Lloyd W. Hillman (email: HillmanL@UAH.edu)

INSTITUTION: The University of Alabama in Huntsville

GRANT NUMBER: N00014-99-1-0226

AWARD PERIOD: 14 December 1998 - 31 December 2001

REPORTING PERIOD: 14 December 1998 - 31 December 2001

OBJECTIVE: The ultimate objectives in this effort are:

- to demonstrate and construct an eye oximeter (EOX) instrument and produce a design suitable for battlefield and trauma bay use
- to investigate and test the efficacy, utility, and value of eye oximetry for treatment of combat casualties with respect to assessment, diagnostics, intervention, and monitoring.

APPROACH: An EOX is an instrument that scans low-powered lasers into a subject's eye and spectroscopically determines the oxygen saturation of the blood within the retinal veins and arteries. Pilot animal studies performed by our group with an EOX indicate that retinal venous oxygen saturation is a sensitive indicator of blood loss. Our research efforts are divided into three basic categories: Instrument Development and Construction, the Medical Science of Retinal Oximetry, and the Optical Science of Retinal Oximetry.

ACCOMPLISHMENTS: A series of theoretical studies, instrument development, and experiments, which have been fully documented in previously submitted annual reports, have yielded significant advances in the science of retinal oximetry. Building on these gains in the final phase of this grant, the Instrument Development and Construction effort has lead to the current device, EOX-2, which has been modified and upgraded for a variety of studies. This instrument utilizes 4 laser sources; three laser diodes and one fiber-coupled argon-ion laser. These lasers are collimated, co-aligned, and sent through the illumination optics to a pair of orthogonal scanning mirrors. These mirrors provide the raster scanning to the beams which pass through an objective lens, and into the pupil of the eye under test. At this point, the light interacts with the vessels and fundus. As the scattered light passes out of the eye's pupil, it is captured by the same objective lens, de-scanned by the mirrors, and sent back through the same illumination optics until it encounters a beamsplitter which directs the light into a high speed PMT. In order to properly synchronize the system, a sophisticated software package and additional electronics have all been integrated. This software tracks the scanning mirrors, fires the lasers such that a wavelength-interlaced image is generated, and notifies the data acquisition system when to grab and store the data sets. And after the data is acquired, it can be analyzed by a variety of codes developed in-house.

The EOX-2 is, in many respects, a modular instrument which provides many configurable options. One variable in the EOX-2 is the use of a variety of laser sources spanning the waveband of 488nm - 830nm. Another modification implemented a preliminary confocal filtering scheme using either pinholes of various diameters or opaque spots (the inverse of a pinhole). The addition of a linear polarizer in the detection path was also implemented to eliminate surface reflections that overwhelmed the desired signal. All of these modifications were developed to provide a deeper understanding of the precise interaction between the incident light and the ocular fundus. They have assisted in improving the system signal to noise ratio, and specifying the actual path of the light collected back from the eye. For example, the collected light could be reflected from the vessel wall, scattered back from the blood volume, reflected back from the fundus after passing through the vessel, or transmitted through the vessel after passing

through once and reflecting from the fundus. By developing an instrument which can probe various wavelengths and use confocal techniques and polarization to constrain the potential sources of collected light, the light - tissue interaction can be accurately examined. This insures that the algorithms operating on the collected data can be properly tuned to the situation.

This device was brought to the U.S. Army Institute of Surgical Research in San Antonio, TX for human studies on subjects in a lower body negative pressure (LBNP) experiment in July 2001 in cooperation with Dr.Victor Convertino. There were several immediate results worth noting. First, the device readily acquired analyzable scans on 15/15 subjects in the short measurement time allotted for the EOX (typically on the order of 30 seconds). This is an indication of its ease of use and potential field use. Second, the LBNP model was successfully used to decrease cardiac output in awake, unsedated/medicated humans safely and repetitively while the EOX data was acquired. Third, no medication to dilate the pupils of the subjects was required.

In addition to enhancements to the EOX, the team developed an improved model eye for *in vitro* testing. The model is a surrogate eye which is used to both test out the EOX instrument itself, and to explore the physics of retinal oximetry in a reduced-variable environment. The model eye provides a6mm pupil diameter, 17mm effective focal length system in which blood filled capillaries, on the order of 100μm in diameter, are situated in front of a sheet of Spectralon. The Spectralon provides uniform homogeneous reflectance and acts as a simplified fundus. Reflectances of 10% to 100% are commercially available and have been used as variables in EOX studies. By providing blood samples with variable but precisely known oxygenation and hemoglobin concentration parameters, we have been able to acquire data sets for large multi-dimensional matrices using the model eye system. Data collection across varying oxygen saturation, hemoglobin concentration, vessel diameter, fundus reflectivity, and filtering configurations permits analysis of the contributions of each of these components to the actual complex measurement . This data has been critical to improving our understanding of the algorithms necessary for calibrating the EOX.

Finally, there have been additional numerical simulations, theoretical analyses, and experiments to improve our knowledge of the scattering and absorption of light passing through blood products. These have included investigations in Mie theory, numerical Monte-Carlo based ray-traces through optical code-based models of blood products, and actual measurements of scattering and absorption.

SIGNIFICANCE: The ability to rapidly and non-invasively, and easily identify occult blood loss would be an invaluable adjunct to the management of the combat casualty. Conventional vital signs (blood pressure and pulse rate) are prone to compensatory maintenance during hemorrhage and are particularly unreliable in the early period of blood loss, when intervention is most efficacious. The alteration of vital signs seen in response to the cascade of acidosis, vascular collapse, and death occurs late in the process of exsanguination and is variable from patient to patient. Invasive techniques, such as oximetric pulmonary artery catheters, are not well suited for battlefield medicine due the time, difficulty, and training level required for placement. A retinal vessel oximeter may be a valuable tool for monitoring blood loss in combat casualties.

The retina is a uniquely optically accessible central perfusion bed. Ophthalmologists and retinal physiologists have long been challenged to devise instrumentation to measure oxygen saturation of hemoglobin in large retinal vessels. Challenges have included inappropriate retinal cameras, a lack of effective calibration, and an insufficient optical sophistication to solve these problems. We have made significant progress toward our goal. We have developed a wavelength selection protocol based on the optical properties of the eye, tested concepts in a model eye of our own design and tested our system on swine and humans.

RECENT PUBLICATIONS:

Kurt R. Denninghoff, Matthew H. Smith, Ph.D., Art Lompado, Ph.D., Lloyd W. Hillman, Ph.D., "Retinal Venous Oxygen Saturation and Cardiac Output During Controlled Hemorrhage and Resuscitation," Submitted to the Journal of Applied Physiology.